A NOVEL NQO1 SPECIFIC ANTI-TUMOR AGENT, SBSC-S3001, SELECTIVELY REGRESSES THE GROWTH OF TUMORS WITH HIGH NQO1 EXPRESSION

Abstract 733 Figure 1 Unsupervised analysis of primary hgPCa that develop metastasis. Features used for unsupervised classification into Cluster 1 and Cluster 2 are: IHC CDB+ cell proximity to tumor cells (ICH_Infiltrated/Desert/Excluded), CDB+ overall cell density in tumor area, MHC1 IHC H-score in tumor (% of tumor cells that are positive X stain intensity), RNAseq signatures for AR pathway in tumor, T-cell exhaustion, Interferon-γ, Macrophage M1, Neuroendocrine phenotypes and DNA repair pathway. Patient cohort annotated for at least one mutations in driver genes (TP53, RHPN2, KMT2D), percent tumor expression of MHC1 IHC (>25% high, <25% low), CD8 infiltration type in relation to tumor and cancer subtypes as defined by Mortensen mRNA profiling (Mortensen et al, Science Reports 2015).

compared to lgPCa. Assessment of MHC-I deficiency by IHC and mRNA revealed that hgPCa has significantly lower MHC-I protein expression compared to lgPCa. Interestingly, MHC-I loss in hgPCa associated with a T-cell exclusion phenotype. Moreover, RNAseq gene expression signatures revealed higher expression of tumor-associated macrophage (TAMs), T-regs, Cancer-Associated Fibroblasts (CAFs), DNA damage repair (DDR) genes and lower Interferon-γ (IFN-γ) expression in hgPCa compared to lgPCa. Overall, hgPCa is characterized by a combined phenotype of ‘MHC1loss/IFN-γ low/CAFhigh/ TAMhigh/T-reghigh/DDRhigh’. 2. Comparisons within hgPCa that develop metastasis: Unsupervised analysis of molecular features in hgPCa patients that developed metastases identified a subset of patients that exhibit a less immunosuppressive phenotype with lower tumor AR expression, retained tumor MHC-I expression, moderate CD8+ T-cell infiltration and a high IFN-γ RNA signature (figure 1), suggesting potential benefit from ICB therapy.

Conclusions Our analysis suggests that hgPCa is characterized by low antigenicity as assessed by loss of MHC-I protein expression and an immunosuppressive microenvironment rich in CAFs, macrophages, T-regs and T-cell exclusion phenotypes. Unlike lgPCa, hgPCa can have a poor prognosis (within 5 years relapse). However, a subset of hgPCa patients that metastasized while on SOC exhibited a biomarker profile that might benefit from combination of SOC with ICB.

Ethics Approval This study was approved by BMS Cambridge Massachusetts Institutional Biosafety Committee, approval number CAM_2020_12050.6

Consent ‘Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.’